## REMARKS

### Status of the Claims

Claims 10-23, 30-35 and 37-41 are pending.

Claims 10 and 17 are rejected under 35 U.S.C. § 102.

Claim 41 is objected to.

Claims 10-23, 30-35 and 37-41 are rejected under 35 U.S.C. 112.

### Amendments

Applicants believe that no new matter has been added to the specification, nor have the amendments broadened the scope of the claims. Basis for the amendments can be found in the claims as originally filed and throughout the instant specification.

### Claim Objections

The Examiner has stated that the subject matter of Claim 41 is allowable, but is rejected as being dependent upon a rejected base claim. Applicants believe that the present amendments make the base claim allowable and believe the rejection is now moot.

### Section 112 Rejections

Applicants gratefully acknowledge the withdrawal of the previous rejections under 35 U.S.C. 112, second paragraph. However, the Examiner has newly rejected the claims 10-23, 30-35 and 37-41 under U.S.C. 35, 112 first paragraph under 35 U.S.C. 112, first paragraph for lack of written description because of the following:

First, the Examiner contends that the negative proviso added in the last amendment has no basis in the disclosure. In response, Applicants have amended the claims to remove the provisos added in the last amendment, and deleted the term "cyano" in the definition of $R^2$. The amended $R^2$ definition also rendered provisos and b at the end of claim 10 unnecessary and these sections of the original proviso were also cancelled. These amendments have basis in the Examples and claims as originally filed, and do not add new matter, nor broaden the scope of the claims. The Applicants believe these amendments render the new rejection under 35 U.S.C. 112 moot, as well as the Examiner's previous rejection of claims 10 and 17 under 35 U.S.C. 102(b) over Tanaka et al.,

Latham et al., and Bradbury et al. Accordingly, Applicants request withdrawal of the aforementioned rejections.

Secondly, the Examiner contends that Claims 30-41, all drawn to methods of treating IMPDH, are indefinite as the Examiner alleges (based on a review article "Papageorgiou") that successful use of the drug would require more than routine experimentation. The Examiner bases his rejection on the statement in the abstract "that except for organ transplant immunosuppression, the treatment of various IMPDH-dependent hyperproliferative diseases by MPA "has failed due to the drug's adverse effect." The Examiner concludes that the use of IMPDH inhibitors has been associated with serious side effects and therefore much more than routine experimentation was necessary to find effective therapeutic formulations. Applicants respectfully traverse.

Throughout the review article there are examples of the successful use of various IMPDH inhibitors including Ribavarin, Mizoribine as well as MPA. The review simply documents efforts that are routine in the art to define side-effects and design formulations around various drawbacks characteristic of new chemical entities. As the review documents, various side effects have been attributed to the structural nature of each type of IMPDH inhibitor and are unique to each type of inhibitor. Because Applicants' compounds have a completely novel structural chemotype, as compared to MPA, it is inappropriate to assume that efforts to design formulations will be non-routine. Even if the review article provides proof of non-routine experimentation for the use of MPA (and Applicants do not agree that this is the case), it is even more likely that the use of Applicants' compounds will be completely routine as they have a novel chemotype, distinct from that of MPA, that is likely NOT to demonstrate the unfortunate enterohepatic recirulation as demonstrated by MPA.

Additionally, Applicants claims are limited by the term "a therapeutically effect amount" which has been found an acceptable description for patent purposes. See In re Halleck, 422 F2d 911, 164 USPQ 647 (CCPA 1970). This term has been found by the courts as acceptable guidance for use in patents. According to In re Forman, 230 USPA 546, 547 (PTO Bd. App. And Interf., 1986) the board held that undue experimentation is not determined by a quantitative test because experimentation is permissible, if it is merely routine, or if the specification in question provides enough guidance for use in view of the state of the art. Indeed, the review article provides ample evidence that there is sufficient information known about IMPDH inhibitors that would allow

routine formulation of Applicants' compounds for use in the treatment of IMPDH-associated disorders. It is accordingly requested that the Examiner's rejection of claims 30-41 be withdrawn.

Thirdly, the Examiner contends that there is no evidence of in vitro/in vivo effectiveness in the specification, and therefore challenges the "competent evidence of art-recognized efficacy for intended uses". Applicants respectfully traverse.

Please see the Applicants' statement on page 96, lines 16-19 where evidence of in vitro utility it is clearly stated: "[t]he compounds disclosed herein are capable of inhibiting the enzyme IMPDH at a measurable level, under the above-described assay or an assay which can determine an effect of inhibition of the enzyme IMPDH. Accordingly, there is ample description of the in vitro utility of Applicants compounds and Applicants respectfully request withdrawal of the indefiniteness/utility rejection under 35 U.S.C. 112, second paragraph.

Applicants believe that each of the Examiner's grounds for rejection is properly stated, traversed, accommodated or rendered moot and that the present application is now in condition for allowance.

**FEES**

No fees should be due. However, if it is determined that a fee is due, please charge same to Deposit Account No. 19-3880 in the name of Bristol-Myers Squibb Company.

**SUMMARY**

In view of the foregoing, it is requested that this case proceed to issuance. The Examiner is invited to contact the undersigned if it is believed prosecution could be expedited.

Respectfully submitted,

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